



**IN THE UNITED STATES PATENT & TRADEMARK OFFICE**

Applicant: DeBenedetti, et al.

: Paper No:

Serial No. 09/916,017

: Group Art Unit:

Filed: July 26, 2001

: Examiner:

For: CANCER GENE THERAPY BASED ON TRANSLATIONAL CONTROL OF  
A SUICIDE GENE



26874

PATENT TRADEMARK OFFICE

**SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT**

THE ASSISTANT COMMISSIONER FOR PATENTS  
Washington, D.C. 20231

Dear Sir:

In accordance with 37 C.F.R. §§1.97 and 1.98, Applicant herewith submits certain patent references and other information, which the Patent & Trademark Office may wish to consider in examining the above-identified application. The references and information are provided below, and are also listed on the attached Form PTO-1449.

**REFERENCES**

4,562,155  
5,646,009  
6,020,162  
WO0078803  
WO0140490

**INVENTOR**

Ricciardi, et al  
Rhoads, et al  
Burley, et al  
Proud, et al  
Laliberte

**ISSUE DATE**

December 31, 1985  
July 8, 1997  
February 1, 2000  
December 2, 2000  
June 7, 2001

**OTHER REFERENCES****Reference:**

Dove, Alan; "Gene Therapy -- Work in Progress", Nature Medicine, Vol. 8, No. 7, July 2002.

Eck, Stephen L., "The Prospects for Gene Therapy," <http://www.hosprract.com/genetics/9910mmc.htm>, 4/12/02.

#10/K.T.  
10/31  
Suppl.  
J.D.S

DeFatta, R.J., et al, "Selective killing of cancer cells through translational regulation of the HTK/GCV gene therapy system," <http://www.cancerprev.org/Meetings/2002/Abstracts/1191/533>, 2002.

Nathan, Cherie-Ann, "Technology and/or Marker Testing in a Clinical Setting Research Projects - Molecular Analysis of Surgical Margins with EIF4E in Can," <http://researchportfolio.cancer.gov/cgi-bin/abstract.pl?Term=21&CSO=4.3&ProjectID=20>; (4/12/02).

Nathan, Cherie-Ann, et al., "COX-2 Expression in Dysplasia of the Head and Neck," *Cancer*, Vol. 92, No. 7, October 1, 2001.

Steiner, et al., "Gene therapy for prostate cancer," *Gene Therapy and Molecular Biology*, Vol. 4, pp. 233-248; December, 1999.

Shariat, S.F., et al., "Adenovirus-mediated transfer of inducible caspases: a novel 'death switch' gene therapeutic approach to prostate cancer," <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list.pids=11>; (4/12/02).

Ring, C.J., et al., "Suicide gene expression induced in tumour cells transduced with recombinant adenoviral, retroviral and plasmid vectors containing the ERBB2 promoter," <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list.pids=89>; (4/12/02).

Martinez-Salas, Encarnacion, "Internal ribosome entry site biology and its use in expression vectors," *Biotechnology*, 10:458-464; 1999.

Taylor, Diane, "Inhibition of eIF4E using mimetic peptides in cells induces apoptosis without affecting transcription," *Research and Innovation Services*.

Quiucho, Florante A., et al, "Structural basis of mRNA cap recognition by proteins," *Structural Biology*, 10:78-86; 2000.

Burley, Stephen K., "Eukaryotic Gene Regulation and Molecular Recognition," *Zhoward Hughes Medical Institute*, <http://www.hhmi.org/research/investigators/burley.html>; (3/19/02).

Guba, Markus, et al, "Rapamycin inhibits primary and metastatic tumor growth by antiangiogenesis: involvement of vascular endothelial growth factor," *Nature Medicine*, Vol. 8, No. 2, February, 2002.

Raught, Brian, et al, "The target of rapamycin (TOR) proteins," *PNAS*, Vol. 98, No. 13, 7037-7044; June 19, 2001.

Polunovsky, Vitaly A., et al., "A Novel Approach to Increase Breast Cancer Chemosensitivity: Disruption of the Anti-Apoptotic Function of Translation Factor eIF4E - Order," <http://65.105.56.185/mater3/category21/A162983.html>; (3/19/02).

Seif, Isabelle, et al., "The Genome of Human Papovavirus BKV," *Cell*, Vol. 18, 963-977, December 1979.

De Benedetti, Arrigo, et al., "Novel BK virus-based episomal vector for expression of foreign genes in mammalian cells," *Nucleic Acids Research*, Vol. 19, No. 8, 1924-1931; (1991).

Johannes, Gregg, et al., "Identification of eukaryotic mRNAs that are translated at reduced cap binding complex eIF4F concentrations using a cDNA microarray," *PNAS*, Vol. 96, No. 23, 13118-13123; November 9, 1999.

van der Velden, Alike W., et al, "The role of the 5' untranslated region of an mRNA in translation regulation during development," *Biochemistry & Cell Biology*, 31, 87-106 (1999).

Barve, Shirish S., "Mechanism of Differential Regulation of IL-2 in Murine Th1 and Th2 T Cell Subsets," *Journal of Immunology*, 1172-1181 (1994).

Hentze, Matthias W., "Translational regulation: versatile mechanisms for metabolic and developmental control," *Cell Biology*, 7:393-398; (1995).

McKendrick, Linda, et al, " Translation initiation factor 4E," *Biochemistry & Cell Biology*, 31:31-35; (1999).

Pestova, Tatyana V., "Molecular mechanisms of translation initiation in eukaryotes," *PNAS*, Vol. 98, No. 13, 7029-7036, June 19, 2001.

Rau, Michael, et al, "A Reevaluation of the Cap-binding Protein, eIF4E, as a Rate-limiting Factor for Initiation of Translation in Reticulocyte Lysate," *Journal of Biological Chemistry*, Vol. 271, No. 15, 8983-8990; April 12, 1996.

De Benedetti, Arrigo, et al, "Overexpression of eukaryotic protein synthesis initiation factor 4E in HeLa cells results in aberrant growth and morphology," *Proc. Natl. Acad. Sci. USA*, Vol. 87, pp. 8212-8216, November, 1990.

Rinker-Schaeffer, Carrie W., "Decreasing the Level of Translation Initiation Factor 4E with Antisense RNA Causes Reversal of *ras*-Mediated Transformation and Tumorigenesis of Cloned Rat Embryo Fibroblasts," *Int. J. Cancer*; 55, 841-847 (1993).

Graff, Jeremy R., "Reduction of Translation Initiation FAC Decreases the Malignancy of *ras*-Transfo Cloned Rat Embryo Fibroblasts," *Int. J. Cancer*; 60, 255-263 (1995).

Graff, Jeremy R., "Translation of ODC mRNA and Polyamine Transport are Suppressed in *ras*-Transformed CREB Cells by Depleting Translation Initiation Factor 4E," *Biochemical and Biophysical Research Communications*, 240, 15-20 (1997).

Sonenberg, Nahum, "Translation factors as effectors of cell growth and tumorigenesis," *Cell Biology* 5:955-960 (1993).

Lazaris-Karatzas, Anthoula, et al, "Malignant transformation by a eukaryotic initiation factor subunit that binds to mRNA 5' cap," *Nature*, Vol. 345, June 7, 1990.

RECEIVED  
OCT 31 2002  
TECH CENTER 1600/2900

Sonenberg, Nahum, et al., "The mRNA 5' cap-binding protein eIF4E and control of cell growth," *Cell Biology*, 10:286-275 (1998).

Raught, Brian, et al., "eIF4E activity is regulated at multiple levels," *Journal of Biochemistry and Cell Biology*, 31:43-57 (1999).

Rosenwald, Igor B., "Deregulation of protein synthesis as a mechanism of neoplastic transformation," *BioEssays*, Vol. 18, No. 3, 243-250 (1996).

Rosenwald, Igor B., "Growth factor-independent expression of the gene encoding eukaryotic translation initiation factor 4E in transformed cell lines," *Cancer Letters*, 98:77-82 (1995).

Rosenwald, Igor B., "Upregulated expression of the genes encoding translation initiation factors 3IF-4E and eIF-2 $\alpha$  in transformed cells," *Cancer Letters*, 102:113-123; (1996).

Willis, Anne E., "Translational control of growth factor and proto-oncogene expression," *Biochemistry & Cell Biology*, 31:73-86 (1999).

Zimmer, Stephen G., et al., "Translational Control of Malignancy: the mRNA cap-Binding Protein, eIF-4E, as a Central Regulator of Tumor Formation, Growth, Invasion and Metastasis," *Anticancer Research*, 20:1343-1352 (2000).

Nathan, Cherie -Ann O., et al., "Expression of eIF4E During Head and Neck Tumorigenesis: Possible Role in Angiogenesis," *Laryngoscope*, 109:1253-1258; August, 1999.

Li, Benjamin D. L., et al., "Overexpression of Eukaryotic Initiation Factor 4E (eIF4E) in Breast Carcinoma," *Cancer*, Vol. 79, No. 12, June 15, 1997.

Keene, Jack D., "Ribonucleoprotein infrastructure regulating the flow of genetic information between the genome and the proteome," *PNAS*, Vol. 98, No. 13, 7018-7024; June 19, 2001.

Schmidt, Emmett V., "The role of *c-myc* in cellular growth control," *Oncogene*, 18:2988-2996 (1999).

Keiper, Brett D., et al., "Protein synthesis initiation factor 4G," *Biochemistry & Cell Biology*, 31:37-41; (1999).

Hoick, Martin, et al., "Internal ribosome initiation of translation and the control of cell death," *TIG*, Vol. 16, No. 10, October, 2000.

Kimball, Scot R., "Eukaryotic initiation factor eIF2," *Biochemistry & Cell Biology*, 31:25-29 (1999).

McCormick, F., "Cancer gene therapy: fringe or cutting edge?" *Nature Rev. Cancer*, 1(2):130-41 (2001).

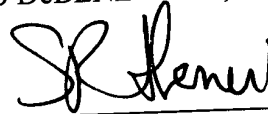
Miller, A.D., "Human gene therapy comes of age," *Nature*, 357:455-460 (1992).

A copy of the listed references are provided. No representation is made or intended that a prior art search has been made or that no better art than that listed is available.

The Assistant Commissioner for Patents is authorized to charge any deficiency or credit any overpayment to Frost Brown Todd LLC Deposit Account No. 06-2226.

Respectfully submitted,

ARRIGO DeBENEDETTI, et al.

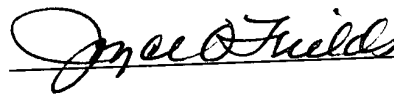


Stephen R. Albainy-Jenei  
Registration No. 41,487  
Telephone (513) 651-6839  
FROST BROWN TODD LLC  
2200 PNC Center  
201 East Fifth Street  
Cincinnati, Ohio 45202-4182

October 24, 2002

**CERTIFICATE OF MAILING**

I hereby certify that a copy of this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to The Assistant Commissioner of Patents, Washington, D.C. 20231 this 24th day of October, 2002.



CINlibrary/1229138.1

Dove, Alan; "Gene Therapy -- Work in Progress", *Nature Medicine*, Vol. 8, No. 7, July 2002.

Eck, Stephen L., "The Prospects for Gene Therapy," <http://www.hosprract.com/genetics/9910mmc.htm>, 4/12/02.

DeFatta, R.J., et al, "Selective killing of cancer cells through translational regulation of the HTK/GCV gene therapy system," <http://www.cancerprev.org/Meetings/2002/Abstracts/1191/533>, 2002.

Nathan, Cherie-Ann, "Technology and/or Marker Testing in a Clinical Setting Research Projects - Molecular Analysis of Surgical Margins with EIF4E in Can," <http://researchportfolio.cancer.gov/cgi-bin/abstract.pl?Term=21&CSO=4.3&ProjectID=20>; (4/12/02).

Nathan, Cherie-Ann, et al., "COX-2 Expression in Dysplasia of the Head and Neck," *Cancer*, Vol. 92, No. 7, October 1, 2001.

Steiner, et al., "Gene therapy for prostate cancer," *Gene Therapy and Molecular Biology*, Vol. 4, pp. 233-248; December, 1999.

Shariat, S.F., et al., "Adenovirus-mediated transfer of inducible caspases: a novel 'death switch' gene therapeutic approach to prostate cancer," <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list.pids=11>; (4/12/02).

Ring, C.J., et al., "Suicide gene expression induced in tumour cells transduced with recombinant adenoviral, retroviral and plasmid vectors containing the ERBB2 promoter," <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list.pids=89>; (4/12/02).

Martinez-Salas, Encarnacion, "Internal ribosome entry site biology and its use in expression vectors," *Biotechnology*, 10:458-464; 1999.

Taylor, Diane, "Inhibition of eIF4E using mimetic peptides in cells induces apoptosis without affecting transcription," *Research and Innovation Services*.

Quijcho, Florante A., et al, "Structural basis of mRNA cap recognition by proteins," *Structural Biology*, 10:78-86; 2000.

Burley, Stephen K., "Eukaryotic Gene Regulation and Molecular Recognition," *Zhoward Hughes Medical Institute*, <http://www.hhmi.org/research/investigators/burley.html>; (3/19/02).

Guba, Markus, et al, "Rapamycin inhibits primary and metastatic tumor growth by antiangiogenesis: involvement of vascular endothelial growth factor," *Nature Medicine*, Vol. 8, No. 2, February, 2002.

Raught, Brian, et al, "The target of rapamycin (TOR) proteins," *PNAS*, Vol. 98, No. 13, 7037-7044; June 19, 2001.

Polunovsky, Vitaly A., et al., "A Novel Approach to Increase Breast Cancer Chemosensitivity: Disruption of the Anti-Apoptotic Function of Translation Factor eIF4E Order," <http://65.105.56.185/mater3/category21/A162983.html>; (3/19/02).

Seif, Isabelle, et al., "The Genome of Human Papovavirus BKV," *Cell*, Vol. 18, 963-977, December 1979.

- De Benedetti, Arrigo, et al., "Novel BK virus-based episomal vector for expression of foreign genes in mammalian cells," *Nucleic Acids Research*, Vol. 19, No. 8, 1924-1931; (1991).
- Johannes, Gregg, et al., "Identification of eukaryotic mRNAs that are translated at reduced cap binding complex eIF4F concentrations using a cDNA microarray," *PNAS*, Vol. 96, No. 23, 13118-13123; November 9, 1999.
- van der Velden, Alike W., et al., "The role of the 5' untranslated region of an mRNA in translation regulation during development," *Biochemistry & Cell Biology*, 31, 87-106 (1999).
- Barve, Shirish S., "Mechanism of Differential Regulation of IL-2 in Murine Th1 and Th2 T Cell Subsets," *Journal of Immunology*, 1172-1181 (1994).
- Hentze, Matthias W., "Translational regulation: versatile mechanisms for metabolic and developmental control," *Cell Biology*, 7:393-398; (1995).
- McKendrick, Linda, et al., "Translation initiation factor 4E," *Biochemistry & Cell Biology*, 31:31-35; (1999).
- Pestova, Tatyana V., "Molecular mechanisms of translation initiation in eukaryotes," *PNAS*, Vol. 98, No. 13, 7029-7036, June 19, 2001.
- Rau, Michael, et al., "A Reevaluation of the Cap-binding Protein, eIF4E, as a Rate-limiting Factor for Initiation of Translation in Reticulocyte Lysate," *Journal of Biological Chemistry*, Vol. 271, No. 15, 8983-8990; April 12, 1996.
- De Benedetti, Arrigo, et al., "Overexpression of eukaryotic protein synthesis initiation factor 4E in HeLa cells results in aberrant growth and morphology," *Proc. Natl. Acad. Sci. USA*, Vol. 87, pp. 8212-8216, November, 1990.
- Rinker-Schaeffer, Carrie W., "Decreasing the Level of Translation Initiation Factor 4E with Antisense RNA Causes Reversal of *ras*-Mediated Transformation and Tumorigenesis of Cloned Rat Embryo Fibroblasts," *Int. J. Cancer*; 55, 841-847 (1993).
- Graff, Jeremy R., "Reduction of Translation Initiation FAC Decreases the Malignancy of *ras*-Transfo Cloned Rat Embryo Fibroblasts," *Int. J. Cancer*; 60, 255-263 (1995).
- Graff, Jeremy R., "Translation of ODC mRNA and Polyamine Transport are Suppressed in *ras*-Transformed CREF Cells by Depleting Translation Initiation Factor 4E," *Biochemical and Biophysical Research Communications*, 240, 15-20 (1997).
- Sonenberg, Nahum, "Translation factors as effectors of cell growth and tumorigenesis," *Cell Biology* 5:955-960 (1993).
- Lazaris-Karatzas, Anthoula, et al., "Malignant transformation by a eukaryotic initiation factor subunit that binds to mRNA 5' cap," *Nature*, Vol. 345, June 7, 1990.
- Sonenberg, Nahum, et al., "The mRNA 5' cap-binding protein eIF4E and control of cell growth," *Cell Biology*, 10:286-275 (1998).
- Raught, Brian, et al., "eIF4E activity is regulated at multiple levels," *Journal of Biochemistry and Cell Biology*, 31:43-57 (1999).
- Rosenwald, Igor B., "Deregulation of protein synthesis as a mechanism of neoplastic transformation,"

Rosenwald, Igor B., "Growth factor-independent expression of the gene encoding eukaryotic translation initiation factor 4E in transformed cell lines," *Cancer Letters*, 98:77-82 (1995).

Rosenwald, Igor B., "Upregulated expression of the genes encoding translation initiation factors 3IF-4E and eIF-2 $\alpha$  in transformed cells," *Cancer Letters*, 102:113-123; (1996).

Willis, Anne E., "Translational control of growth factor and proto-oncogene expression," *Biochemistry & Cell Biology*, 31:73-86 (1999).

Zimmer, Stephen G., et al., "Translational Control of Malignancy: the mRNA cap-Binding Protein, eIF-4E, as a Central Regulator of Tumor Formation, Growth, Invasion and Metastasis," *Anticancer Research*, 20:1343-1352 (2000).

Nathan, Cherie -Ann O., et al., "Expression of eIF4E During Head and Neck Tumorigenesis: Possible Role in Angiogenesis," *Laryngoscope*, 109:1253-1258; August, 1999.

Li, Benjamin D. L., et al., "Overexpression of Eukaryotic Initiation Factor 4E (eIF4E) in Breast Carcinoma," *Cancer*, Vol. 79, No. 12, June 15, 1997.

Keene, Jack D., "Ribonucleoprotein infrastructure regulating the flow of genetic information between the genome and the proteome," *PNAS*, Vol. 98, No. 13, 7018-7024; June 19, 2001.

Schmidt, Emmett V., "The role of *c-myc* in cellular growth control," *Oncogene*, 18:2988-2996 (1999).

Keiper, Brett D., et al., "Protein synthesis initiation factor 4G," *Biochemistry & Cell Biology*, 31:37-41; (1999).

Hoick, Martin, et al., "Internal ribosome initiation of translation and the control of cell death," *TIG*, Vol. 16, No. 10, October, 2000.

Kimball, Scot R., "Eukaryotic initiation factor eIF2," *Biochemistry & Cell Biology*, 31:25-29 (1999).

McCormick, F., "Cancer gene therapy: fringe or cutting edge?" *Nature Rev. Cancer*, 1(2):130-41 (2001).

Miller, A.D., "Human gene therapy comes of age," *Nature*, 357:455-460 (1992).

EXAMINER 

DATE CONSIDERED 1.6.03

Page \_\_\_\_ of \_\_\_\_

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.